This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of cystinosis?
   
   If yes, continue to #2.
   
   If no, do not approve.
   
   **DENIAL TEXT:** See the denial text at the end of the guideline.

2. Does the patient require treatment for corneal cystine crystal accumulation?
   
   If yes, **approve for 12 months by GPID with a quantity limit of #4 bottles (15mL each) per 28 days.**
   
   If no, do not approve.
   
   **DENIAL TEXT:** See the denial text at the end of the guideline.

   **DENIAL TEXT:** Approval requires that Cystaran be used in the treatment of corneal cystine crystal accumulation in patients with cystinosis.

RATIONALE

To ensure appropriate use aligned with FDA approved indication.

Instill one drop of Cystaran in each eye, every waking hour. Discard after 1 week of use.

Cystinosis is a metabolic disease characterized by an accumulation of cystine in different organs and tissues, leading to potentially severe organ dysfunction. There are three distinct types of cystinosis: nephropathic (infantile) cystinosis, intermediate (adolescent) cystinosis, and ocular non-nephropathic (adult/benign) cystinosis. Nephropathic cystinosis, which is by far the most common, has been estimated to affect one of every 100,000 to 200,000 children.

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CYSTEAMINE HYDROCHLORIDE

RATIONALE (CONTINUED)

Cystine is a product of protein degradation that is normally transported through the lysosomal membrane to the cytosol. In cystinosis, a defect in the transport system causes cystine to accumulate inside the lysosomes. Since cystine is poorly soluble, crystals form as the cystine concentration increases. Although the adult form of the disease may be limited to ocular symptoms, patients with infantile cystinosis can have both renal and extrarenal symptoms as cystine deposits in the cornea and the conjunctiva can be seen on slit-lamp examination. These deposits are responsible for photophobia, watering, and blepharospasm. Irregular and peripheral depigmentation of the retina is also an early finding. Visual impairment may occur later, in children older than 10 years. Hemorrhagic retinopathy may also be a complication of this disorder. Cysteamine acts as a cystine-depleting agent by entering the cell, reacting with cystine, and forming both cysteine and a cysteine-cysteamine complex, which are able to leave the lysosomes.

The safety and efficacy of Cystaran was evaluated in controlled clinical trials that examined in approximately 300 patients. The primary efficacy end point was the response rate of eyes that had a reduction of at least 1 unit in the photo-rated Corneal Cystine Crystal Score (CCCS) at some time point during the study when baseline CCCS ≥1, or a lack of an increase of more than 1 unit in CCCS throughout the study when baseline CCCS <1.

Study 1 combined the data from three smaller studies. For eyes with a lower baseline of CCCS <1, the response rate was 13% (4/30) [95% CI: (4, 32)]. For eyes with a higher baseline of CCCS ≥1, the response rate was 32% (94/291) [95% CI: (27, 38)].

Study 2 evaluated ocular cystinosis patients who had a baseline of CCCS ≥1. The response rate was 67% (10/15) [95% CI: (38, 88)].

Study 3 also evaluated ocular cystinosis patients; for eyes with a baseline of CCCS ≥1, the response rate was 33% (3/9) [95% CI: (8, 70)].

The most frequently reported ocular adverse reactions occurring in ≥10% of patients were sensitivity to light, redness, and eye pain/irritation, headache and visual field defects. There is a warning for potential association of benign intracranial hypertension (or pseudotumor cerebri) with oral cysteamine treatment. It is uncertain if this condition occurs in those who only use the ophthalmic formulation.

Cystaran is pregnancy category C.

Instill one drop of Cystaran in each eye, every waking hour. Discard after 1 week of use. Patients with contact lenses should remove lenses prior to application of solution and may reinsert lenses 15 minutes following its administration (Cystaran contains benzalkonium chloride, which may be absorbed by soft contact lenses).

CONTINUED ON NEXT PAGE
CYSTEAMINE HYDROCHLORIDE

RATIONALE (CONTINUED)
Each week, one new bottle should be removed from the freezer. Patients should be advised to allow the bottle to thaw completely (approximately 24 hours) prior to use. After the bottle is completely thawed, the patient should record the discard date on the bottle label. The discard date is seven (7) days from the day the bottle is thawed. Patients should be advised to store thawed bottle at 2°C to 25°C (36°F to 77°F) for up to 1 week. The thawed bottles should not be refrozen. To minimize the risk of contamination, do not touch the dropper tip to any surface. Keep bottle tightly closed when not in use.

FDA APPROVED INDICATIONS
Cystaran is a cystine-depleting agent indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

REFERENCES
- Cystaran [Prescribing Information]. Gaithersburg, MD: Sigma Tau Pharmaceuticals; December 2012.

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